Remarks/Arguments

I. Status

Claims 1-36 have been examined. Applicants have canceled claims 2 and 20. Accordingly claims 1, 3-19, and 21-36 are pending. Claim 1 has been amended to incorporate the recitations of claim 2; claim 19 has been amended to incorporate the recitations of claims 20. No new matter has been added by any of the requested amendments.

II. The Information Disclosure Statement

The Examiner has advised that certain references previously submitted to the United States Patent & Trademark Office by Applicants have not been considered apparently because the submitted copies have not been associated with the application files. Applicants herewith submit duplicate copies of these references and respectfully request their consideration.

III. The Rejections Pursuant to 35 U.S.C. § 112

Claims 19-36 have been rejected pursuant to 35 U.S.C. § 112, second paragraph, as indefinite in light of the presence of the term "said analytes" in claim 19.

Applicants have amended claim 19 in order to provide clear antecedent basis for the "said analytes" term, and respectfully submit that such action fully responds to the Examiner's concerns. Accordingly, Applicants submit that the rejection of claims 19-36 pursuant to 35 U.S.C. § 112, second paragraph, may be properly withdrawn.

IV. The Rejections Pursuant to 35 U.S.C. § 103

A. The Rejection of Claims 1-9, 11-13, 16-27, 29-31 and 34-36

Claims 1-9, 11-13, 16-27, 29-31 and 34-36 have been rejected pursuant to 35 U.S.C. § 103(a) as obvious to one of ordinary skill in light of U.S. Patent No. 5,370,777 (**Guttman *et al.* '777**).

Guttman *et al.* '777 is stated to disclose an aqueous gel medium (a non-cross-linked hydrophilic polymer) for facilitating the electrophoretic separation of analytes present in a sample. The Examiner has advised that the pH ranges recited in claim 1 would have been *prima facie* obvious in light of **Guttman *et al.* '777** (which is alleged to teach a pH range of 8.0-8.5, and more specifically a pH of 8.3). The Examiner has additionally advised that claims 2 and 3 are obvious in light of **Guttman *et al.* '777**'s teaching of the use of a reducing reagent. Applicants respectfully traverse and request reconsideration.

Applicants respectfully submit that the present invention is not *prima facie* obvious in light of **Guttman *et al.* '777**. As the Examiner will note, claim 1 recites the **inclusion** of sodium dodecyl sulfate. Contrary to the Examiner's conclusion, **Guttman *et al.* '777** does ***not*** teach conducting the electrophoretic process at a pH of between 8.0 – 8.5 in the presence of sodium dodecyl sulfate. In this regard, Applicants respectfully draw the Examiner's attention to column 13, lines 3-19:

> The pH of the buffer used in conjunction with the dynamically cross-linked composition is principally selected with respect to the type of surfactant utilized. For cationic surfactants, the pH of the buffer should be in the acidic range (i.e. between about 2.0 and 5.0); ***for anionic surfactants, the pH of the buffer should be in the alkaline range (i.e. between about 8.0 and 10.0)***; for nonionic surfactants, the pH of the buffer is between about 5.0 and about 8.0. ***With respect to the preferred SDS surfactant, a most preferred pH is about 8.8.*** (Emphasis Added)

Thus, **Guttman *et al.* '777** teaches that when the anionic surfactant (column 2, line 64) sodium dodecyl sulfate is employed, the electrophoretic process is to be conducted at a pH between about 8.0 and 10.0, and most preferably at 8.8. It is submitted that those of ordinary skill would not have concluded that **Guttman *et al.* '777** teaches or suggests employing the pH range of 8.0 – 8.3 claimed by Applicants. As disclosed in the present specification (page 11, lines 18-19), employing a pH within this range leads to an unexpected improvement in electrophoretic separation and resolution.

Applicants additionally submit that those of ordinary skill would not have concluded that **Guttman *et al.* '777** teaches the inclusion of reagent(s) that function to help keep protein analytes in a reduced form ***in*** the aqueous gel medium as is claimed by Applicants.

In this regard, the Examiner's attention is respectfully directed to column 2, lines 38-41 of **Guttman *et al.* '777**, wherein the patent teaches that in order for proteins to migrate according to their size in capillary electrophoresis, it is necessary to treat the proteins so as to cause them to have the same effective charge-to-mass ratio, and that this can be accomplished using a surfactant. **Guttman *et al.* '777** further teaches that in order to disrupt disulfide linkages and produce proteins having the desired "uniform shape and identical mass to charge ratios," the proteins are to be treated with a reducing reagent (please see column 18, lines 30-32). Thus, it is submitted that those of ordinary skill would have concluded that **Guttman *et al.* '777** teaches the use of a reducing reagent solely for the purpose of sample preparation; i.e., "***before*** introduction into the capillary column" (column 18, lines 41-42, emphasis added).

It is respectfully submitted that Applicants' claims relate not to sample preparation solutions, but to an aqueous gel medium (and a capillary electrophoresis system), and recite the ***inclusion*** of one or more reagent(s) that function to help keep protein analytes in a reduced form ***within*** such medium (and ***within*** the medium of such a system). It is submitted that those of ordinary skill would have concluded that **Guttman *et al.* '777** does ***not*** teach such inclusion since the reducing reagents disclosed by

Guttman *et al.* '777 are uncharged molecular species that accordingly would not migrate into the electrophoretic gel medium under the conditions employed.

Applicants therefore submit that those of ordinary skill would not have found it obvious in light of **Guttman *et al.* '777** to have included reagent(s) that function to help keep protein analytes in a reduced form ***within*** the employed aqueous gel medium. It is submitted that prior to Applicants' invention, the art believed that undesirable peak broadening of proteins subjected to capillary electrophoresis reflected the incomplete disulfide bond reduction of the applied proteins during their preparation for electrophoresis. In contrast, the present invention reflects the finding that disulfide bonds that were reduced during the sample preparation stage can re-oxidize, that such re-oxidation is undesirable, and can be addressed through the inclusion of reducing reagent(s) ***in*** the aqueous gel medium of the electrophoretic column (please see Example 6 of the Specification). It is submitted that **Guttman *et al.* '777** fails to teach or suggest such a finding and fails to teach or suggest such a solution.

In light of Applicants' amendments and the above remarks, Applicants respectfully submit that the rejection of claims 1-9, 11-13, 16-27, 29-31 and 34-36 pursuant to 35 U.S.C. § 103(a) in light of U.S. Patent No. 5,370,777 **(Guttman *et al.* '777)** may now be properly withdrawn.

B. The Rejection of Claims 10 and 28

Claims 10 and 28 have been rejected pursuant to 35 U.S.C. § 103(a) as obvious to one of ordinary skill in light of U.S. Patent No. 5,370,777 **(Guttman *et al.* '777)** in view of U.S. Patent No. 3,622,661 **(King *et al.*)**. King *et al.* is cited as evidence that commercially available dextran possesses a non-cross-linked structure composed of approximately 95% alpha-D-(1-6) linkages. Applicants respectfully traverse and request reconsideration.

Applicants note that although **King *et al.*** discloses the nature and percentage of the dextran linkages, it does not appear to teach the use of dextran compositions having

the molecular weight recited in applicants' claims. **Guttman *et al.* '777** does not remedy this deficiency, since it provides no basis for concluding either the inherency of dextran molecular weights or that the dextran employed by **Guttman *et al.* '777** meets the nature and percentage of the dextran linkages recited in the claims. It is submitted that the teachings of the two documents are not combinable in the manner proposed by the Examiner.

Applicants additionally submit that claims 10 and 28 comprise the recitations of claims 1 and 19, and accordingly are patentable for the reasons stated with respect to such claims the rejections based on **Guttman *et al.* '777**. It is submitted that **King *et al.*** fails to teach or suggest the inclusion of one or more reagent(s) that function to help keep protein analytes in a reduced form ***within*** the aqueous gel medium (and ***within*** the medium of such the claimed capillary electrophoresis), and thus fails to remedy the deficiency of **Guttman *et al.* '777**.

In light of Applicants' amendments and the above remarks, Applicants respectfully submit that the rejection of claims 10 and 28 pursuant to 35 U.S.C. § 103(a) in light of U.S. Patent No. 5,370,777 **(Guttman *et al.* '777)** as combined with U.S. Patent No. 3,622,661 **(King *et al.*)** may now be properly withdrawn.

C. The Rejection of Claims 14-15 and 32-33

Claims 14-15 and 32-33 have been rejected pursuant to 35 U.S.C. § 103(a) as obvious to one of ordinary skill in light of U.S. Patent No. 5,370,777 **(Guttman *et al.* '777)** in view of U.S. Patent No. 5,213,669 **(Guttman '669)**. **Guttman '669** is stated to teach an aqueous gel medium having an alcohol that is glycerol. Applicants respectfully traverse and request reconsideration.

Applicants submit that claims 14-15 and 32-33 comprise the recitations of claims 1 and 19, and accordingly are patentable for the reasons stated with respect to such claims the rejections based on **Guttman *et al.* '777**. It is submitted that **Guttman '669** fails to teach or suggest the inclusion of one or more reagent(s) that function to help keep protein

analytes in a reduced form ***within*** the aqueous gel medium (and ***within*** the medium of such the claimed capillary electrophoresis), and thus fails to remedy the deficiency of **Guttman *et al.* '777**.

In light of Applicants' amendments and the above remarks, Applicants respectfully submit that the rejection of claims 4-15 and 32-33 pursuant to 35 U.S.C. § 103(a) in light of U.S. Patent No. 5,370,777 **(Guttman *et al.* '777)** as combined with U.S. Patent No. 3,622,661 **(King *et al.*)** may now be properly withdrawn.

V. Concluding Remarks

Applicants submit that the present response is complete and complies with the requirements of 35 U.S.C. §121. The Application is believed to be in condition for Allowance and early notice of such favorable action is respectfully requested. Should the Examiner have any remaining questions regarding the subject invention or its patentability, Applicants encourage the Examiner to contact the undersigned to answer such questions or provide any desired additional information.

Respectfully Submitted,

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